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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,729	12/08/2004	Takeshi Nakanishi	441P088	6032

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NIELDS & LEMACK
176 EAST MAIN STREET, SUITE 7
WESTBORO, MA 01581

EXAMINER	
ROGERS, JAMES WILLIAM	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
08/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,729	NAKANISHI ET AL.	
	Examiner	Art Unit	
	James W. Rogers, Ph.D.	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/25/2007 has been entered.

Response to Amendment

Applicant's amendments to the claims filed 05/25/2007 have been entered; claim 1 was amended.

Response to Arguments

Applicant's arguments with respect to claims 1,3-8 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1,3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yokoyama et al. (US 6,080,396, disclosed previosuly) in view of Matsumara (Drug Delivery System, 16, No. 5, 401-408, 2001, disclosed previously) in view of Meir et al. (US 6,916,488 B1).

Yokoyama discloses a pharmaceutical preparation and the method to prepare it containing a copolymer of PEG and a poly amino acid which can include aspartic or glutameric acid as its monomers, the amino acid contains a side chain carboxyl group that can be attached to an anthracyline-based anticancer agent. See abstract, col 3 lin 50-60. The process for producing the composition included dissolving the block copolymer in solvents such as water or water mixed with low-boiling organic solvents such as THF along with the drug, the composition was then concentrated and freeze dried. See col 12 lin 53-col 13 lin 22 and examples. Regarding claims 5 and 7 Yokayama teaches using dimmers, trimers and tetramers of anthracylines such as adriamycin eg doxorubicin as well as drugs other than the dimmers, trimers and

tetramers including adriamycin for incorporation in the block copolymer, thus the limitations for anthracycline and doxorubicin are met. From the disclosure within Yokoyama it is obvious that other techniques could be employed besides dialysis or ultrafiltration because the patent states "replacing the solvent of the mixture solution with water by means of dialysis, ultrafiltration or the like", obviously shows that there are more ways to remove water encompassed within the patents scope. See col 12 lin 64-67. Also from the disclosure of Yokoyama it is obvious that other solvents may be employed besides the listed solvents because the patent states "a mixture solvent thereof and the like". See col 12 lin 54-60.

Yokoyama is silent on what methods other than using dialysis and ultrafiltration to prepare the drug containing copolymer. Yokoyama is also silent on the use of the exact organic solvents as now currently claimed by applicants.

Matsumara is used to show that it was known at the time of the invention that when dialysis or ultrafiltration are conducted on pharmaceuticals with contained drugs part of the drug is also removed, therefore the drug is not used effectively and the drug content cannot be increased. Therefore it would be obvious to use another technique to concentrate drugs instead of ultrafiltration and dialysis. See entire document especially experimental.

Meir is used for the disclosure within that it was already well known in the art at the time of the invention that techniques other than dialysis and ulfiltration were already well known to be used in the art at the time of the invention to concentrate amphiphilic polymer drug compositions, specifically Meir lyophilized the composition. See abstract,

col 10 lin 63-col 12 lin 60. Neither ultrafiltration or dialysis was mentioned in the procedure to purify and concentrate the amphiphilic copolymer drug mixture. Meir is also used to show that numerous solvent systems were well known in the art at the time of the invention to be useful in amphiphilic polymer drug compositions, specifically Meir disclosed the use of DMF, DMSO, ethanol, methanol, THF, halogenated hydrocarbons, acetone and mixtures of suitable solvents such as water and an alcohol. Thus it would be obvious to one of ordinary skill in the art that the above solvents are interchangeable with one another for the purpose of making amphiphilic polymer/drug compositions. Thus the claimed solvents in applicants invention would have been *prima facie* obvious because the substitution of one known element such as the solvents disclosed within Yokoyama for another known element such as the solvents disclosed within Meir would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

It would have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to combine the art described in the documents above because while Yokoyama discloses dialysis and ultrafiltration to prepare the drug containing copolymer from Matsumara one skilled in the art would be motivated to try another technique to concentrate so that drug content is not lost and Meir showed that other methods besides dialysis or ultrafiltration in the production of drug copolymer compositions such as lyphiliazation were well known at the time of the invention. The motivation to combine the above documents would be a general method to improve the drug loading of a block copolymer-drug containing a hydrophobic portion including PEG

and a hydrophilic portion that includes polyamino acids that are covalently bonded through a condensation reaction with an anthracylcycline. Thus, the claimed invention, taken as a whole was *prima facie* obvious over the combined teachings of the prior art.

Claims 1,3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakurai et al. (EP 0,397,307 A2) in view of Matsumara (Drug Delivery System, 16, No. 5, 401-408, 2001, disclosed as background art by applicants) in view of Meir et al. (US 6,916,488 B1).

Sakurai discloses a water soluble block copolymer and the method to make it, the copolymer contains a hydrophobic segment that can contain PEG and a hydrophobic section that can contain polyaspartic acid and polyglutamic acid, the amino acid has a side chain carboxyl group that can be attached to an anthracyline-based anticancer agent including adriamycin eg doxorubicin. See abstract and pag 5 lin 3-14 and examples. The process for producing the composition included dissolving the block copolymer, adding the drug dissolved in DMF, then adding EDC and stirring the solution for 19 hours. Regarding claim 8 Sakurai discloses that the synthesized high molecular drug, despite the high adriamycin-substitution ratio, demonstrated good water solubility and kept its water solubility even when lyophilized or concentrated, therefore from this statement it is obvious that Sakurai lyophilized the copolymer-drug.

Sakurai is silent on what methods other than using dialysis and ultrafiltration to prepare the drug containing copolymer. Sakurai is also silent on the use of the exact organic solvents as now currently claimed by applicants.

Matsumara is used to show that it was known at the time of the invention that when dialysis or ultrafiltration are conducted on pharmaceuticals with contained drugs part of the drug is also removed, therefore the drug is not used effectively and the drug content cannot be increased. See entire document especially experimental. Therefore it would be obvious to use another technique to concentrate drugs instead of ultrafiltration and dialysis.

Meir is used for the disclosure within that it was already well known in the art at the time of the invention that techniques other than dialysis and ultrafiltration were already well known to be used in the art at the time of the invention to concentrate amphiphilic polymer drug compositions, specifically Meir lyophilized the composition. See abstract, col 10 lin 63-col 12 lin 60. ` Meir is also used to show that numerous solvent systems were well known in the art at the time of the invention to be useful in amphiphilic polymer drug compositions, specifically Meir disclosed the use of DMF, DMSO, ethanol, methanol, THF, halogenated hydrocarbons, acetone and mixtures of suitable solvents such as water and an alcohol. Thus it would be obvious to one of ordinary skill in the art that the above solvents are interchangeable with one another for the purpose of making amphiphilic polymer/drug compositions. Thus the claimed solvents in applicants invention would have been *prima facie* obvious because the substitution of one known element such as the solvents disclosed within Sakurai for another known element such as the solvents disclosed within Meir would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

It would have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to combine the art described in the documents above because while Sakurai discloses dialysis and ultrafiltration to prepare the drug containing copolymer from Matsumara one skilled in the art would be motivated to try another technique to concentrate so that drug content is not lost and Meir showed that other methods besides dialysis or ultrafiltration in the production of drug copolymer compositions such as lyphiliazation were well known at the time of the invention. The motivation to combine the above documents would be a general method to improve the drug loading of a block copolymer-drug containing a hydrophobic portion including PEG and a hydrophilic portion that includes polyamino acids that are covalently bonded through a condensation reaction with an anthracylcycline. Thus, the claimed invention, taken as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to James W. Rogers, Ph.D. whose telephone number is (571) 272-7838. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER